

ORIGINAL RESEARCH ARTICLE

Correlation of biological cervical cancer with its demographic and obstetric parameters in Ain Defla region, Algeria

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Abstract

This study aims to determine the prevalence of cervical dysplasia and its relationship to biological and demographic characteristics. A transversal observational study is based on 236 conventional smears collected in Algeria. A Pap smear was taken, fixed and then stained using Papanicolaou staining. The interpretation of the results was done using the Bethesda 2014 system. Some of the patients with abnormal smears had colposcopy and, if necessary, a biopsy. Other patients with low-grade lesions were recommended to have their smears resumed 6 months or 1 year later. Cytological analysis was performed for 236 patients. Among those, 94 patients had abnormal smears, 45 cases with ASCUS (19.06 %), LSIL was reported in 36 cases (15.25%), AGC was observed in 6 cases (2.54 %), HSIL in 4 cases (1.69 %), only 1(0.42 %) case observed in SCC and 2 cases in ADK (0.84 %). Also, 34 low-grade patients underwent cytological examination 6 months to 1 year later to determine the persistence, regression or progression of low-grade dysplasia. During follow-up, persistence was observed in 35.29% (n= 12) of cases, progression to high-grade squamous intraepithelial lesion (HSIL) was detected in 5.88% (n= 2), while 52.88% (n= 20) of the patients experienced regression. Moreover, the frequency of Pap smear positivity correlated with the duration of OC use, the duration of marriage and parity. In this study, the prevalence of abnormal smear was 39.84 % for cytology. The colposcopy and histology confirmed just 3.33%. Meanwhile, these results highlight the importance of early screening of this pathology. (*Afr J Reprod Health* 2022; 26[10]: 31-37).

Keywords: Cervical cancer, dysplasia, pap smear, prevalence, epidemiology, Algeria

Résumé

Cette étude vise à déterminer la prévalence de la dysplasie cervicale et sa relation avec les caractéristiques biologiques et démographiques. Une étude observationnelle transversale est basée sur 236 frottis conventionnels collectés en Algérie. Un frottis de Pap a été prélevé, fixé puis coloré à l'aide de la coloration de Papanicolaou. L'interprétation des résultats a été faite à l'aide du système Bethesda 2014. Certains des patients présentant des frottis anormaux ont eu une coloscopie et, si nécessaire, une biopsie. Il a été recommandé aux autres patients présentant des lésions de bas grade de reprendre leurs frottis 6 mois ou 1 an plus tard. L'analyse cytologique a été réalisée pour 236 patients. Parmi ceux-ci, 94 patients avaient des frottis anormaux, 45 cas avec ASCUS (19,06 %), LSIL a été rapporté dans 36 cas (15,25 %), AGC a été observé dans 6 cas (2,54 %), HSIL dans 4 cas (1,69 %), seulement 1 cas (0,42 %) observé dans SCC et 2 cas dans ADK (0,84 %). De plus, 34 patients de bas grade ont subi un examen cytologique 6 mois à 1 an plus tard pour déterminer la persistance, la régression ou la progression de la dysplasie de bas grade. Au cours du suivi, une persistance a été observée dans 35,29 % (n= 12) des cas, une progression vers une lésion malpighienne intraépithéliale de haut grade (HSIL) a été détectée dans 5,88 % (n= 2), tandis que 52,88 % (n= 20) des les patients ont connu une régression. De plus, la fréquence de positivité du frottis Pap était corrélée avec la durée d'utilisation des CO, la durée du mariage et la parité. Dans cette étude, la prévalence des frottis anormaux était de 39,84 % pour la cytologie. La coloscopie et l'histologie n'ont confirmé que 3,33 %. Parallèlement, ces résultats soulignent l'importance d'un dépistage précoce de cette pathologie. (*Afr J Reprod Health* 2022; 26[10]: 31-37).

Mots-clés: Cancer du col de l'utérus, dysplasie, test de Pap, prévalence, épidémiologie, Algérie

Introduction

In Africa, cervical cancer is the most common cancer among women, with a high prevalence in the 15 to 44 age group. Most of them belong to the most disadvantaged population^{1,2}.

More than 90% of all observed cervical cancer cases are related to persistent high-risk human papillomavirus (HPV-HR) infection, resulting in precancerous lesions that can progress to invasive cervical cancer if left untreated^{1,3-5}. Screening by performing a regular cervico-vaginal smear can

detect precancerous lesions and treat them at an early stage⁶. The cytology-based screening strategy is the most widely used technique to detect precancerous lesions. It has been shown that it decreases the incidence of invasive cancers and mortality in most countries⁷. The objective of this study -strictly limited to the region of Ain Defla - is to provide a prevalence of cervical dysplasia in Algeria from 236 systematically screened patients and to correlate the results with biological, demographic and obstetrics characteristics. Moreover, we examined the concordance between cytologic and histologic analysis and evaluated persistence, progression, and regression in patients with low-grade dysplasia.

Methods

Population surveyed and samples collection

The transversal observational study was carried out from January to June 2020, 236 cervical smears were collected and analyzed from Algerian women aged between 22 and 65, who consulted the oncology department and the anatomical pathology laboratory at Ain Defla Hospital, Algeria. After including participants who met the eligibility criteria and obtaining written informed consent, study subjects were interviewed using a structured questionnaire that considers demographic and obstetrical characteristics.

A written informed consent was obtained from all participants, and the study was approved by the Medical School Research Ethics Board at the Health and Population Branch. Work was conducted in accordance with the World Medical Association's Code of Ethics for studies involving human subjects.

Cytology

Cervical cytology is confirmed by a conventional smear, which is the most frequently used method in cytology screening programs⁸⁻¹². The spatula was inserted into the cervical opening and rotated to collect a sample of endocervix cells. A second sample is also taken from the surface of the cervix "the ectocervix" as part of the Papanicolaou smear (Pap smear)^{13,14}. Fixation of the smear was made on a glass slide with 95% alcohol for 15 minutes. The slide was stained using the Papanicolaou dye at the hospital's Antipathy department. Finally, results

were interpreted by implementing the Bethesda 2014 system which is a reporting system for smear results and cervical or vaginal cytological changes¹⁵⁻¹⁸.

Histology, colposcopy and control smears

Based on the result of the Pap smear, some patients with low-grade dysplasia are advised to have a follow-up Pap smear 6 months or a year later, while others are referred directly for colposcopy. Patients with abnormal colposcopy underwent biopsy. Those whose control smears revealed persistent dysplasia underwent colposcopy and, if necessary, biopsy at the Anatomical pathology laboratory of Ain Defla Hospital. For those whose smears revealed high-grade squamous intraepithelial lesion (HSIL), colposcopy and, if necessary, biopsy were performed. The samples were analyzed at the histopathology laboratory of the main hospital to confirm or invalidate the grade of the lesion revealed by the smear. Patients with low-grade squamous intraepithelial lesion (LSIL) who did not undergo colposcopy were seen at the health center of 'Algiers' for a follow-up smear.

Data analysis

Statistical analysis was performed using SPSS version 17. Independent samples t-test was used to compare the means of different variables. Data were presented as mean \pm standard deviation (SD). The results were considered statistically significant when the two-tailed *p* value was < 0.05 .

Results

Cytology

The census of different cases with cervical lesions was carried out on a series of smears (236 smears) according to the number of cases of each lesion. Abnormal smears were found in 94 cases (39.84 %) out of 236, 45 cases with Atypical squamous cells of undetermined significance (ASCUS) (19.06 %), LSIL was reported in 36 cases (15.25%), AGC (typical glandular cells of undetermined significance) was observed in 6 cases (2.54 %), HSIL in 4 cases (1.69 %), 2 cases observed in adenocarcinoma (ADK) (0.84 %) and only one case (0.42%) in squamous cell carcinoma (SCC) (Table 1).

Table1: Frequency of abnormal Pap smear results in the overall study population

Pap smear result	All patients
Count (%)	236 (100%)
Negative for intraepithelial lesion	142 (60.16%)
Positive for intraepithelial lesion	94 (39.84%)
ASCUS	45 (19.06%)
LSIL	36 (15.25%)
AGC	6 (2.54%)
HSIL	4 (1.69%)
ADK	2 (0.84%)
SCC	1 (0.42%)

Table2: Histology reports

Tests (Histology)	Values N (%)
Total biopsy (%)	60 (100%)
unsatisfactory	2 (3.33%)
Cervicitis	8 (13.33%)
polyps	6 (10%)
LSIL	19 (31.66%)
HSIL	13 (21.66%)
carcinoma	2 (3.33%)
normal	10 (16.66%)

Exploration of cytological lesions presented by the Papanicolaou technique allowed us to distinguish the superficial exocervical cells stained in pink and the intermediate cells stained in blue (Figure1).

Histology and colposcopy

Among patients with low-grade lesions (LSIL) and patients with ASCUS, 79 had performed colposcopy, 19 were normal and 60 had abnormalities. Moreover, biopsies were performed on those with abnormalities, of which 2 were unsatisfactory, 10 had normal histology, 8 patients had cervicitis, 6 had a polyp, 19 had a low-grade lesion, 13 had a high-grade lesion, and 2 had carcinoma (Table 2).

Persistence, progression and regression of the LSIL

In this study, 34 patients with low-grade dysplasia were referred to the cytology unit of Ain Defla for a follow-up smear 6 months or 1 year later to determine persistence, regression or progression of the dysplasia. During follow-up, persistence was observed in 35.29% (n=12) of cases, progression to HSIL in 5.88% (n=2) and regression in 52.88% (n=20) of patients.

Comparison of Pap smear-positive and Pap smear-negative patients with respect to demographic and obstetric data

Our results show that patient age, length of marriage and duration of oral contraceptive (OC) use are higher in patients with positive Pap smears, with a highly significant statistical difference between the two Pap smear groups ($P > 0.001$). Moreover, most of the abnormal Pap smear positive patients (85.10%) have a parity >3 , with a highly significant statistical difference between the two groups ($P > 0.001$), while there was no statistical significance regarding the mode of previous deliveries ($P = 0.333$ (NS) (Table 3). It is also shown, in Table 3, that there is a statistically significant association between duration of OC use and high grades of cervical cytology in the Pap smear ($P = 0.046$); the longer the duration of OC use, the greater the degree of abnormal cervical cytology (Table 3).

Discussion

In Algeria, cervical cancer is the second gynecological cancer, with an incidence of 8.7 per 100 000 women. It represents 12.5% of all female cancers. It is a real public health problem¹⁹. The estimated participation rate for cervical cancer screening in Ain Defla is very low (5.85% of women aged 18-68), especially in rural areas and among the elderly (only 1.45% of women over 40). There is no reliable estimate of the prevalence of cervical dysplasia or risk factors for cervical dysplasia specific to Ain Defla rural region.

This study reported that the median age of patients with a positive Pap smear was 47, which is higher than that of patients with a negative Pap smear (35). Moreover, the frequency of positive Pap smear results increased with the duration of marriage with a statistically significant difference ($p < 0.001$). In agreement with the present study, Wang *et al*²⁰ found that the incidence of cervical epithelial changes was higher in patients aged 56 to 65 than in those aged 36 to 45.

Our study shows that LSIL cases decreased by 52.88% and the progression rate was 5.88%. Concerning the persistence of dysplasia, which is one of the main causes of cancer occurrence, it is 35.29% in our study. These differences could be explained, on the one hand, by the delay of patients

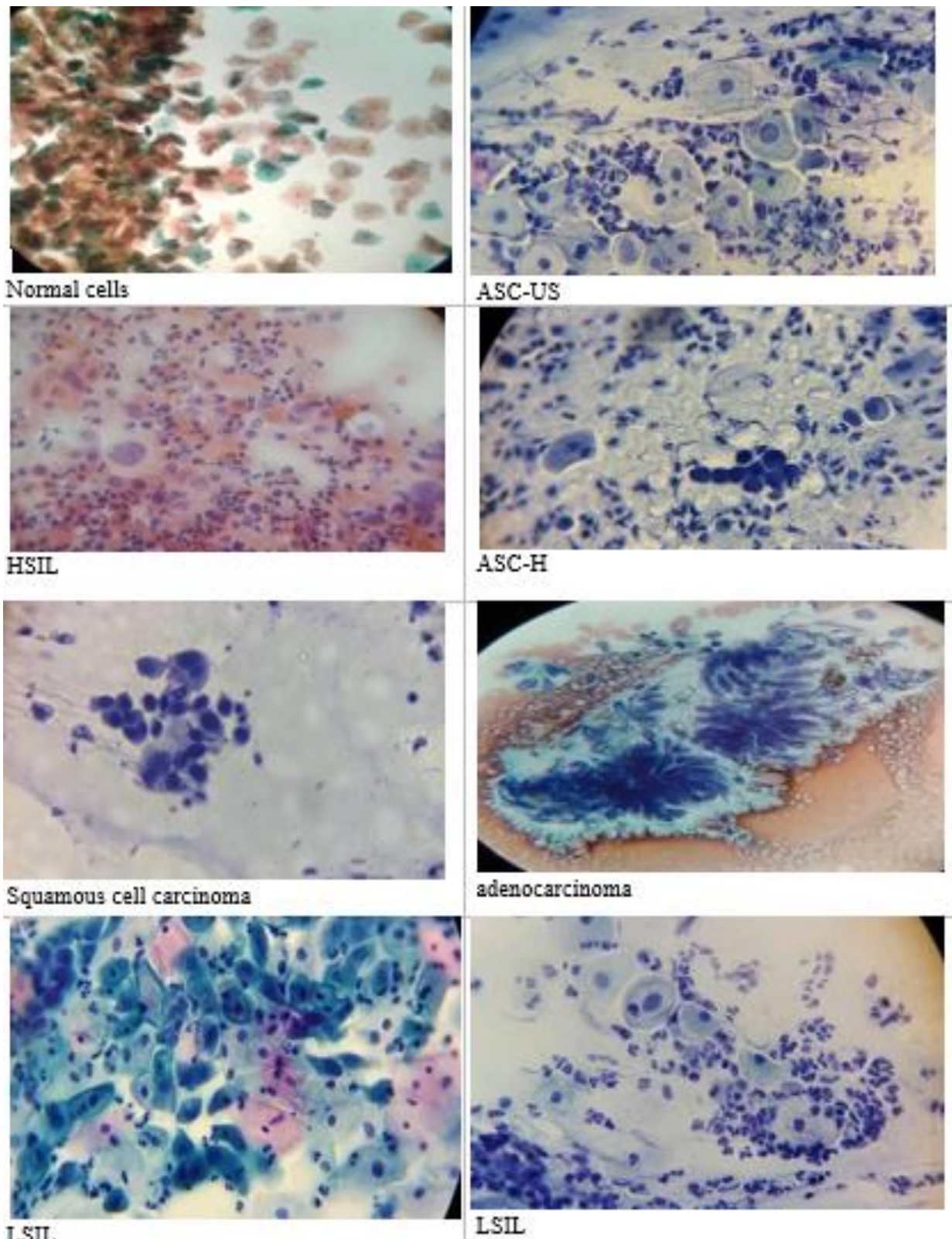


Figure1: Cytological lesions

Table 3. Comparison between patients with positive and negative Pap smear regarding the demographic and obstetric data

Demographic and obstetric data	Abnormal Pap smear		Normal Pap smear		P-value (Sig.)		
Count	94 (39%)		142 (60.16%)				
Demographic data							
Age (years)							
Median (Range)	47 (30– 65)		35(22– 40)		<0.001		
Duration of marriage (years)							
Median (Range)	29 (18– 48)		19 (7– 22)		<0.001		
Obstetric data							
Parity							
≤ 3	14 (14.9%)		95 (66.91%)		<0.001		
>3	80 (85.10%)		47 (33.09%)				
Mode of previous deliveries							
Caesarean section (CS)	8 (8.25%)		54 (38.03%)		0.333		
Vaginal delivery (VD)	86 (91.48%)		88 (61.97%)				
COCs use duration (years)							
Median (Range)	9 (5– 13)		6 (5– 7)		<0.001		
Gynecological data							
	ASCUS	LSIL	AGC	HSIL	ADK	SCC	P-Value(Sig.)
Count	45	36	6	4	2	1	
OCs use duration (years)	7.7 ± 1.5	7.8 ± 0.7	8.9 ± 0.8	10.7 ± 2.1	9.08 ± 0.0	9.0 ± 0	0.048
Mean ± SD							

with abnormal cytology before being called for biopsy, sometimes from 6 months to 1 year or more, which could lead to a regression of LSIL to a large extent or to a progression to HSIL. On the other hand, this difference could also be explained by the technical problems related to the sample quality or errors related to reading or coloring. These shortfalls could also be justified, in part, by the very expensive funding to cover the costs of histology and the availability of the colposcope.

In the present study, the frequency of Pap-positive smears increased with parity (84.2% for parity < 3 versus 15.8 % for parity ≤ 3), and the result was statistically significant ($p < 0.001$). In agreement with our results, El-Moselhy *et al.*²¹ observed that multiparity, which is less than 5 (< 5), is a significant risk factor for cervical epithelial changes (31.4 % in the CIN group and 14 % in the non-CIN group). Moreover, multiparity is considered as a risk factor for cervical cancer (CC), particularly in human papillomavirus (HPV)-positive women²². The relative risk (RR) of CC in women with five or more births ranged from 3.8 (in squamous cell carcinoma)²³ to 4.4²⁴ in studies, compared with nulliparous women, or 5.1 compared with nulliparous or primiparous women²⁵.

In this study, among patients with a positive Pap smear, 54 patients diagnosed had

caesarean section (CS) and 88 patients had only vaginal deliveries (VD), whereas among patients with a negative Pap smear, 8 patients had CS and 86 patients had only vaginal deliveries, with a P value of 0.33 that was not significant. However, El-Moselhy *et al.*²¹ declared that vaginal delivery is a significant risk factor for cervical neoplasia. In CIN group ($n=49$), normal vaginal delivery was in 47 cases. In normal group ($n=92$), normal vaginal delivery was in 67 cases (OR= 8.77, 95% ECL: 2.0-79.08).

In the present study, the frequency of Pap smear positivity correlated with the duration of OC use, with the median duration of OC use in Pap smear-positive patients being 8 years versus 6 years in Pap smear-positive patients. There is a positive relationship between the duration of OC use and the degree of cervical injury. The average duration of OC use in patients with a positive Pap smear was 7.7 ± 1.5 years for ASCUS, 7.8 ± 0.7 years for LSIL, 10.7 ± 2.1 years for HSIL 9.08 ± 0.0 years for ADK and 9.0 ± 0 years for SCC.

Oh *et al.*²⁶ confirmed our results that OC use for more than 5 years is a significant risk factor for positive Pap smear results. Moreover, both OC use and IUD use were associated with an increased risk of developing CIN3+. However, for women with a contraceptive wish, an IUD seems safer than an OC as the risk of developing CIN3+ and cervical cancer was higher for OC users^{27,28}.

Conclusion

Cervical cancer is a significant female reproductive health problem, especially in developing countries where it constitutes the major cause of death. This study focused on the cytological lesion of such cancer. A positive association was found between age, the duration of marriage, parity, the duration of oral contraceptive use and abnormal Pap smear. As well, a positive association between long-term use of OC and a higher grade of abnormal Pap smear has been identified. We suggest, through our study, to provide Ain Defla region with screening programs which require sufficient funds, adequate infrastructure and resources to screen all eligible women.

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Authors' contribution

AL conceived and carried out statistical analysis as well as manuscript editing. AL, SH, MA, AKS made data collection and manuscript writing. Finally, AL, SH, MA, AKS and FL reviewed and approved the manuscript.

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